REMARKS

The Office Action dated June 1, 2004 presents the examination of claims 7-12, 15, 17, 19-20, and 28-29. Claim 16 is withdrawn from consideration. Claims 7, 8, and 15 are canceled herein. Claims 9-12, 16-17, 19-20, and 28 are amended. Support for subject matter added to claims 11 and 12 is found in the specification, such as on page 8, lines 15-21 and page 21, lines 3-15. No new matter is inserted into the application.

Election/Restriction

The Examiner maintains the restriction requirement such that claim 16 is withdrawn from consideration. Applicants respectfully traverse the withdrawal of claim 16. Reconsideration of the claim and withdrawal of the restriction requirement are respectfully requested.

Applicants respectfully request that the Examiner rejoin claim 16 to the examined claims. Claim 16, as amended, is directed to peptides shown in any one of SEQ ID NOs: 19-21, which are specific embodiments of "an isolated tumor antigen peptide which comprises a sequence selected from an amino acid sequence shown in any one of SEQ ID NOs: 3-5 wherein the amino acid residue at position 2 is substituted by tyrosine, phenylalanine, methionine, or tryptophan,

and/or the C-terminus is substituted by phenylalanine, leucine, isoleucine, tryptophan, or methionine, and which has the functionally equivalent properties" as defined in currently amended claim 12. Accordingly, if claim 12 is about to be allowed, claim 16 should be rejoined or taken into consideration.

For all of these reasons, Applicants respectfully request that the Examiner withdraw the restriction requirement with regard to claim 16, and examine the claim in the present application.

Rejection under 35 U.S.C. § 112, first paragraph

Written Description

The Examiner maintains the rejection of claims 9-12, 15, 17, 19-20, and 28-29 under 35 U.S.C. § 112, first paragraph, for allegedly lacking proper written description. Claims 7, 8, and 15 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner maintains his argument that the specification does not provide adequate written description for "derivatives." In order to expedite allowance of the present application, but not to acquiescence to the Examiner's rejection, reference to

"derivatives" in claims 9, 10, 16, 17, 19, and 28 is deleted. Further, the term "derivative" in claims 11 and 12 is amended to recite specific isolated tumor antigen peptides having an amino acid sequence shown in any one of SEQ ID NOs: 3-18 wherein the amino acid residue at position 2 is substituted by tyrosine, phenylalanine, methionine, or tryptophan, and/or the C-terminus is substituted by phenylalanine, leucine, isoleucine, tryptophan, or methionine. Support for these substitutions is found in the specification, such as on page 8, lines 15-21, and page 21, lines 3-15. Since the amended claims no longer recite "derivatives," the instant rejection is overcome.

The Examiner also implies that the phrase "peptides of 8-14 amino acids in length" also fails to meet the written description requirements. Applicants respectfully disagree. The phrase "peptide of 8 to 14 amino acids in length" describes a tumor antigen peptide that binds to an HLA antigen and is recognized by cytotoxic T lymphocytes. The present invention is based, in part, on the finding that the protein shown in SEQ ID NO: 1 (ART-1), the function of which was previously unknown, is a tumor antigen protein which gives rise to tumor antigen peptides via intracellular processing. It is known in the art that the process for determining whether a protein is a tumor antigen protein is

difficult. However, once a protein is found to be a tumor antigen protein, methods for identifying and preparing tumor antigen peptides from the tumor antigen protein are well known in the art and within the skill of the average artisan.

As evidence thereof, Applicants attach hereto as Exhibit 1 a copy of Rammensee et al., *Immunogenetics,* 41:178-228, 1995, which is mentioned on page 21 of the specification. Rammensee et al. provides a compendium of MHC peptide motifs and MHC ligands known to date, as well as a discussion of methods used to determine binding motifs and ligands. Further, Table 1 on page 21, lines 7 to 13 of the instant specification contains the binding motifs necessary for peptides to bind HLA antigens. The specification also provides Examples which demonstrate that some of the "peptides of 8 to 14 amino acids in length" according to the present invention function as tumor antigen peptides (See Examples 4 to 9).

Therefore, given the disclosure of the specification as well as knowledge in the art, the "peptides of 8-14 amino acids in length" falling within the scope of the instant claims can be readily identified and prepared by those skilled in the art. Accordingly, the instant claims fully comply with the written description requirement under 35 U.S.C. 112, first paragraph with respect to the phrase "peptide of 8 to 14 amino acids in length."

Further, on page 4 of the Office Action, the Examiner asserts that the amino acid sequences represented by SEQ ID NOs: 3-5 do not have a core sequence which can be specifically correlated or which is predictable so as to be representative of the broad class of fragments claimed. Applicants respectfully point out that the Examiner's assertion is incorrect. The peptides represented by SEQ ID NOs: 3-5 do possess common features in that they (1) are derived from the same protein ART-1 (SEQ ID NO: 1), and (2) have a binding motif necessary to bind HLA antigens as defined in Rammensee et al. and Table 1 of the present specification. Therefore, contrary to the Examiner's assertions, the peptides represented by SEQ ID NOs: 3-5 possess common features which are representative of the class of peptides claimed.

For all of the above reasons, Applicants respectfully submit that the instant claims are fully described in the specification such that the requirements of 35 U.S.C. § 112, first paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Enablement

The Examiner maintains the rejection of claims 7-8, 17, and 20 under 35 U.S.C. § 112, first paragraph, for allegedly not being

enabled by the specification. Claims 7 and 8 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

In order to expedite prosecution of the present application, but not to acquiesce to the Examiner's position, the term "pharmaceutical" in claims 17 and 20 is deleted. Thus, the instant rejection is overcome.

Rejection under 35 U.S.C. § 102

Nagase et al.

The Examiner maintains the rejection of claims 9-12 and 15 under 35 U.S.C. § 102(b) as allegedly being anticipated by Nagase et al. Claim 15 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Independent claim 9, as amended, is directed to an isolated tumor antigen peptide of 8 to 14 amino acids in length that is a fragment of the amino acid sequence of SEQ ID NO:1, and that binds to an HLA antigen and is recognized by cytotoxic T lymphocytes.

Nagase et al. fails to anticipate the instant claim 9, and claims dependent thereon.

On page 4 of the Office Action, the Examiner asserts that because the Nagase et al. teaches a cDNA encoding a protein that is identical to SEQ ID NO:1, any peptide fragment of SEQ ID NO:1 would be anticipated. Further, the Examiner asserts that although an amino acid sequence of 8 to 14 amino acids is not recognized by Nagase et al. as an independent fragment, the claims as currently written to not preclude sequences found endogenously in SEQ ID NO:1.

Applicants strongly disagree and respectfully point out that the Examiner's assertions are contrary to established case law. Simply put, Nagase et al. fails to describe any peptide of 8 to 14 amino acids in length. Further, Nagase et al. fails to describe either the function or the activity of the peptide having the claimed amino acid sequence. The Examiner is reminded that when evaluating the scope of a claim, **every limitation** in the claim must be considered. In re Ochiai, 71 F.3d 1565 (Fed. Cir. 1995). Further, a claim is anticipated only if **each and every element** as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628 (Fed. Cir. 1987). Since

Nagase et al. fails to disclose a peptide of 8 to 14 amino acids in length, and fails to describe the function peptide as a tumor antigen peptide, Nagase et al. fails to describe each and every element of claim 9. Accordingly, Nagase et al. fails to anticipate claim 9, and claims dependent thereon.

As at least acknowledged by the Examiner, Nagase et al. fails to recognize a tumor antigen peptide of 8 to 14 amino acids in length. Based on this assumption it is clear that nothing in the prior art would have led the skilled artisan to select the particular sequence corresponding to 8 to 14 amino acids of SEQ ID NO: 1 out of the cDNA sequences disclosed by Nagase et al. The mere existence of an open reading frame, followed by a prediction of protein-coding regions of the cDNA clones, with no function ascribed to the encoded protein, does not provide a reason for the skilled artisan to produce a tumor antigen peptide having 8 to 14 amino acids.

For all of the above reasons, Applicants respectfully submit that Nagase et al. fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner newly rejects claims 7-8, 17, and 20 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Claims 7 and 8 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner argues that the makeup of the composition recited in the claims is unclear since a "composition" implies more than one component. Applicants respectfully submit that the Examiner's assertion is incorrect. As evidence thereof, the definition of "composition" provided by Merriam-Webster Online is attached hereto as Exhibit 2. See Merriam-Webster Online at http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=composition&x=14&y=14. The Examiner's attention is drawn to the second definition of "composition," which is defined as "the manner in which something is composed; the qualitative and quantitative makeup of a chemical compound." Thus, contrary to the Examiner's assertions, the correct usage of the term "composition" in the chemical arts does not necessarily imply more than one component.

Furthermore, Applicants respectfully point out that the composition of claim 17 comprises as an active ingredient at least

one of substances selected from the isolated tumor antigen peptides according to any one of claims 9 to 12 and 16, and the composition of claim 20 comprises as an active ingredient the recombinant polypeptide of claim 19. The transition term "comprising" is inclusive or open-ended and does not exclude additional, non-recited elements. U.S. Pat. & Trademark Off., *Manual Pat. Examining Proc.* § 2111.03 (8th ed. Rev. 2 2004). Thus, the composition of claim 17, for example, is not limited only to at least one of substances selected from the isolated tumor antigen peptides according to any one of claims 9 to 12 and 16, but also includes other non-recited elements. Genentech, Inc. v. Chiron Corp., 112 F.3d 495 (Fed. Cir. 1997).

For all of the above reasons, the rejection is improper. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner newly rejects claims 7-8 and 28 under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the instant specification. Claims 7 and 8 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the

rejection of claim 28. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Claim 28 recites *E. coli* JM109 (3D9) (deposit number FERM BP-6929). The Examiner asserts that the specification does not provide evidence that the deposits are either: (1) known and readily available to the public; (2) reproducible from the description in the specification; or (3) deposited in an acceptable public repository.

FERM BP-6929 is deposited at The National Institute of Bioscience and Human Technology (1-1-3 Higashi, Tsukuba, Ibaraki, Japan). The National Institute of Bioscience and Human Technology is an International Depository Authority (IDA) established under the Budapest Treaty, as shown in the English portion of the Declaration of Deposit. A copy of the Declaration of Deposit with the English portion highlighted is attached hereto as Exhibit 3. Although not specifically mentioned by the Examiner, cell lines KG-CTL and KE-4 are also deposited at the National Institute of Bioscience and Human Technology. KG-CTL is deposited as FERM BP-6725 (see Exhibit 4, attached hereto) and cell line KE-4 is deposited as FERM BP-5955 (see Exhibit 5, attached hereto). Cell lines KG-CTL and KE-4 are disclosed in the specification on pages 5 and 45, respectively.

Applicants' representative hereby states that the cell lines of *E. coli* JM109 (3D9) (FERM BP-6929), KG-CTL (FERM BP-6725), and KE-4 (FERM BP-5955) are deposited under the Budapest Treaty, that each cell line will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, and that each cell line will be replaced should it ever become non-viable.

For all of the above reasons, the criteria for deposit of biological material set forth in 37 C.F.R. §§ 1.801-1.809 are fully satisfied. Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above amendments and/or remarks fully address and overcome and/or render moot the objections/rejections of record. The present application is in condition for allowance. The Examiner is respectfully requested to issue a Notice of Allowance indicating that claims 9-12, 16-17, 19-20, and 28 are allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at

the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
John W. Bailey, #32,881

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

JWB/KLR
0020-4872P

Attachments: Exhibit 1 (*Immunogenetics*, 41:178, 1995)
Exhibits 2-5 (Certificates of deposit)